TETANUS.

A STUDY OF THE NATURE, EXCITANT, LESIONS, SYMPTOMATOLOGY, AND TREATMENT OF THE DISEASE, WITH A CRITICAL SUMMARY OF THE RESULTS OF SERUM THERAPY.

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THE literature upon tetanus for the past ten years is scattered through the journals of all countries and nationalities; and, with rare exceptions only, a majority of these articles belong to the class of casuistic material. This is particularly true since the discoveries of Tizzoni and Cattani and Behring, which in one measure, at least, mark an epoch-making period in the therapy of tetanus. That this subject cannot as yet be considered a closed one is well evidenced by the fact that there does not as yet exist any decided unanimity, either as regards the pathogenesis or the pathological anatomy, or the therapy of the affection. Although tetanus is one of the diseases that has been known almost from time immemorial, and has been studied by scientific men of all ages, it is really only since the discovery of the specific bacillus by Nicolaier in 1884 that the study of tetanus has received a scientific foundation.

Nature and Varieties of Tetanus.—It may be well at the outset to define tetanus as an acute infectious disease, which is invariably and indubitably caused by the entrance into the body of the specific micro-organism, the Bacillus tetani, discovered by Nicolaier in 1884, and first cultivated in pure culture by Kitasato in 1891 in an anaërobic medium.

[1] Read at the meeting of the New York County Medical Society, April 23, 1900.

Many different varieties are reported upon and described, and have received different names, as tetanus traumaticus, tetanus cephalicus, tetanus puerperalis, tetanus neonatorum, tetanus rheumaticus, tetanus idiopathicus, etc.; but all that can be said of them is, that they are in substance merely varieties of tetanus, which differ only in the place of infection, and as a result may give rise to slight differences in progress and symptomatology. Presuming, however, and of this in the present light of bacteriology and animal experiment, there cannot be the slightest doubt that true tetanus is and must always be caused by the bacillus of Nicolaier, there is certainly no place in the description of a given case of tetanus for the diagnosis "rheumatic" or "idiopathic." The mildest interpretation that can be put is, that in a certain number of cases, fortunately a very small number, either the point of infection has not been searched for with the requisite amount of care, or that it has not been found. That this is quite within the range of possibility is well proven by the fact that tetanus has followed such minute injuries as the introduction of a hypodermic needle, of which there are a number of cases recorded, or the sting of a bee, or a leechbite,[1] which may have healed or apparently healed long before the outbreak of the tetanic symptoms.

It would be proper to require with every diagnosis of tetanus the finding of the bacillus of Nicolaier, but being anaërobic, and in other respects also not easy of cultivation, it would be too much to expect of every general practitioner into whose care these cases mostly come, an exact bacteriological diagnosis. Furthermore, the symptoms in every case of acute tetanus are so well marked and so precise, that none could be mistaken. It is far easier to err on the other side and call a case tetanus which may not be one; carious teeth, periostitis, and osteomyelitis of the jaw, tonsillar and peritonsillar abscesses have been and may be mistaken for tetanus; but in none of these can there be any true symptoms of tetanus;

[1] Tetanus bacilli were found in the snout of a leech by Pacinotti, quoted by Honl.[1]

and it would be manifestly improper to base the diagnosis of tetanus merely upon the locking of the jaws.

Symptomatology.—As a characteristic example of the symptoms of acute tetanus, I cannot do better than describe the case which has come under my observation.

S. G., eighteen years old, a cutter by occupation, was admitted in the evening of July 11, 1899, to the surgical division of Mount Sinai Hospital, with the following history:

On July 4, the patient shot himself in the palm of the hand with a blank cartridge. He immediately applied for treatment at a hospital, at which the wound was disinfected and bandaged; some of the wad was supposed to have been removed at this time. Subsequently, the wound was treated by his family physician, and of the course of the wound between this time and his admission to the hospital only the following facts can be ascertained with a certain degree of accuracy,—moderate discharge from the wound, accompanied by very little pain or tenderness; the fingers were continuously kept in a flexed position, as any attempt at extension was accompanied by pain. On the morning of the 11th (seven days after the injury), the patient noticed for the first time a rigidity of the jaw, with pain at the temporo-maxillary articulation when attempts were made to force the jaws apart; difficulty in swallowing.

Status præsens: Temperature, 99.3° F.; pulse, 90; respirations, 20. Fairly well nourished, rather anæmic individual, who does not give the impression of impending serious illness. In the palmar surface of the left hand, corresponding to the metacarpal bone of the middle finger, a round wound about two or three millimetres in width, the edges of which are covered with a grayish-black deposit; on pressure a small amount of grayish pus oozes from this opening; the fingers are flexed upon the hand and the hand upon the forearm; rigidity of the masseter and temporal muscles, evidenced by the fact that the teeth cannot be separated to a greater distance than about two centimetres; some rigidity also of the muscles of the back of the neck, as the patient cannot approximate the chin to the sternum.

Shortly after admission, at 9 P.M., under cocaine anæsthesia, an incision about one and a half inches long was made over the seat of the infection, and the entire area exposed; the wad of

the cartridge, or at least the greatest part of it, was found still at the bottom of the cavity and was removed; the wall of this cavity had a grayish burned color and contained a large amount of burned powder. Cultures taken from the pus and examined by Dr. Liebman, assistant pathologist of the hospital, gave a negative result; cover-glass preparations revealed a variety of germs, but no unmistakable tetanus bacilli were found. The entire cavity was disinfected with 1:500 mercuric chloride solution and a liberal gauze dressing of a weaker solution applied. Internally, sodium bromide and chloral hydrate in thirty and fifteen grain doses respectively were given *pro re nata*.

Between the time of the operation and the following afternoon all the symptoms became progressively more marked; the abdominal muscles were by this time also more or less in a state of contraction, but as yet no alarming symptoms had arisen. At 2 P.M. the dressing was changed and packed with Lugol's solution: the patient received also an intravenous injection of twenty cubic centimetres antitoxin (Paris Institute Pasteur), and at 8 P.M. ten cubic centimetres, while the internal medication of morphine, chloral, and sodium bromide was continued. At this time the patient complained of considerable pain in the back; the muscles of the neck, back, and abdomen were painful and in a state of tonic contraction, with intense pain, cramp like in character; risus sardonicus was marked; the teeth could not be separated for a distance greater than a finger's breadth; there occurred also at short intervals sudden and painful contractions of the masseter muscles, the teeth at such time injuring the tongue. Patient can only swallow in gulps, and at those times only with the greatest difficulty; on this account the sodium bromide and chloral were from this time on administered per rectum, dissolved in forty cubic centimetres physiological salt solution.

During the night there was no remission in the progress of the disease; on the contrary, all symptoms became more marked, and this determined me upon injecting the antitoxin intracerebrally.

At 9.30 A.M. of July 13, under chloroform anæsthesia, a small incision was made, and after drilling with the electric trephine a small opening through the skull, three cubic centimetres of the tetanus antitoxin were injected through a fine hypodermic needle into the anterior lobe. This procedure was repeated on the left

side, using two cubic centimetres of the antitoxin. About seven minutes were consumed for the actual injection on each side.

The patient took the anæsthetic well; pulse and respiration being good throughout; the muscles were well relaxed. On waking, the patient complained constantly of pain, with recurring exacerbations, every ten minutes, cramp like in character. At 4 P.M. the temperature rose to 102.3° F. and the pulse-rate to 130; the rectal medication was continued. There was no diminution of the symptoms after the operation, and at 10.30 P.M. the patient had a clonic convulsion lasting five seconds, which started with a twitching of the facial muscles, becoming general almost immediately, every muscle being apparently affected; the movements were irregular, the body being thrown from one side of the bed to the other. Temperature, 104.4°; pulse, 166. After the convulsion all the muscles were soft and relaxed, the jaws being separable to a distance greater than at any time since the onset of the disease. Patient apparently comatose and does not answer questions, but wakes up at frequent intervals, with a sharp groan, evidently in great pain. At 12.10 A.M. of July 14 the patient had two more convulsions, with marked opisthotonos; when the second attack ceased, the pulse became more rapid and breathing slow and stertorous, and a few minutes later ceased entirely.

A limited autopsy, eighteen hours post mortem, performed by Dr. Mandlebaum, pathologist to the Hospital, showed the following: Marked rigor mortis; in the palm of the left hand an incised wound (site of infection), free from pus and free from any gross changes. From each parietal a small button of bone (five millimetres in diameter) has been removed; dura not adherent, but at site of openings congested. The vessels on the convex surface of the brain distended; fresh thrombi in the longitudinal and lateral sinus, and in the circle of Willis; brain tissue very soft and easily indented; on the right side there was an area of congestion in the pia corresponding to the opening in the parietal bones. The spinal cord showed no gross changes. The microscopical findings will be published on a subsequent occasion.

From a point of prognosis this case belongs to the very worst class; the period of incubation was practically only six days, and its course after the onset of the tetanic symptoms was characterized only by a most acute progress, as there was

not at any time the slightest diminution of the untoward symptoms. The antitoxin was used quite early, the patient receiving the first injection barely seventeen hours after admission to the Hospital, and less than thirty hours after the first appearance of the tetanic symptoms.

The pathological anatomy is not yet fully known in spite of numerous autopsies; many of the recorded autopsies give merely the gross pathological changes in some of the viscera, and show in general insufficient observation. It is to be hoped that the more recent methods of examination of the minute structural changes will throw more light on this subject. Before the advent of this method of examination, the recorded autopsies speak of inflammation and degeneration of the peripheral nerves; anæmia and hyperæmia of the brain and spinal cord; meningeal hæmorrhages; hypertrophic changes of the glia; multiplication of the nuclei in the interstitial connective tissue; inflammatory changes in the sympathetic nervous system.

Autopsies on tetanus patients by competent and trained observers are of so unfrequent occurrence that not much opportunity has as yet been given for the study of the minute structural changes, in the light of modern research; fortunately, however, the lesions of experimental tetanus on tetanized rabbits are so much like those in human tetanus that important analogies can be deduced. A great deal of systematic and valuable work has of late been done by Goldscheider and Flatau, which tends to clear up many of the mooted points regarding the effect of the toxines of tetanus on the nervous system.

Goldscheider and Flatau,[19] in studying the spinal cords of experimentally tetanized rabbits, constantly found certain characteristic changes in the motor cells of the anterior horns, which in the order of their development depend upon the concentration and virulence of the toxins injected and upon the duration of the infection. These changes are readily recognizable by Nissl's method of staining and show primarily an enlargement of the nucleus, which at the same time becomes

more indistinct; then there follows an enlargement and disintegration of Nissl's cell-granules, with an enlargement of all the nerve cells. These authors also found, which is an important hint in respect to the therapy, that when antitoxin has been used, it had a distinct retarding influence on these changes. Goldscheider and Flatau in a subsequent publication [20] verified these changes on the spinal cord of a patient who died of tetanus. Almost similar or only in minor details different results were obtained by Matthes,[21] Westphal,[22] Goebel,[23] and Tauber.[24] The changes related above are characteristic of tetanus and are constantly found.

Our present knowledge of the pathogenesis of tetanus points with great probability to the anterior horns of the spinal cord as the primary seat of origin for the tetanic contractions; hence the constant and characteristic morphologieal changes found in these cells by Goldscheider and Flatau bear a most important relation to the nature and development of tetanus. It is, however, much to be regretted that our knowledge respecting the structure of the ganglion cells under physiological conditions is still insufficient; while the value of Nissl cell granules is not yet firmly established and universally accepted.

Up to the time of the discovery of the tetanus bacillus by Nicolaier [25] and the successful isolation of the toxins by Brieger and Cohn, Kitasato, etc., the study of tetanus was limited to occasional, few and far between, autopsies at hospitals with attached pathological laboratories, and, as already stated, came to no definite conclusion, and did not aid materially in clearing up the nature of tetanus. Since then, the successful experimental inoculation of the disease into animals, at first by Carle and Rattone in 1884, gave us continual means for the closer study of its pathogenesis.

Stintzing [20 27] lays particular stress upon the fact that in all forms of experimental tetanus there is always found, before the disease has been fully developed, a contraction of the muscles in that part of the body where the infection has taken place. This is the so-called local tetanus; and he says

that it has never been observed in human tetanus. As a matter of fact, there is not the slightest doubt in my mind that it does occur also at an early stage in human tetanus, only that it is frequently overlooked on account of the fact that, as a rule, we but rarely have an opportunity to see the affected patient at so early a stage, since we get them only when the disease is far more advanced, and when this symptom has already disappeared. It certainly was one of the marked symptoms in the case under my observation, and was so pronounced that even the patient himself, otherwise of but a fair order of intelligence, distinctly so stated it in the anamnesis, without my calling his attention to this point.

This local tetanus occurs regularly and without exception in all cases of experimental tetanus, and consists of regular contractions and rigidity in the muscles nearest to the seat of infection, while the remaining muscles are affected only much later. If the intoxication is only of a milder character, the tetanus may even remain limited to the first group of muscles, without involving the rest of the body.

The explanation of this local tetanus is by no means easy, and was an important point in the research of tetanus, and even now is not entirely a settled matter.

At first it was definitely decided that the brain is not the place of origin for the tetanic spasms, as it was shown by decapitation that animals still continued to have the tetanic spasms, so there remained only the normal reflex arch, *i.e.*, sensory nerves, spinal cord, motor nerves, and muscles.

Muscles and motor nerves have been excluded by curare and division experiments.

The experiments of Autokratow, which were confirmed by Conrmont and Doyon (*loc. cit.*), lay considerable stress upon the sensory nerves, as these experimenters have found that tetanus did not arise after division of the sensory nerves leading from the extremity experimented upon. A directly opposite result, however, was obtained by Brunner [28] [29] [30] [31] and Gumprecht;[32] as these observers found that local tetanus did

arise when the posterior nerve-roots belonging to the sensory nerves leading from the extremity experimented upon were divided. (Gumprecht explains this important divergence in the results by the possibility that in the experiments of Courmont and Doyon there remain motor nerve-roots, or by a diminished reflex irritability, due to a lowering of the vitality, induced by the extent of the operation.) With such conflicting evidence, it is certainly more proper to give more weight to the positive results of Brunner and Gumprecht than to the negative results of Courmont and Doyon. If this is accepted as proven, there remains only the spinal cord, which must be looked upon as the source of the tetanic spasms. Brunner finishes his *résumé* by stating that if the spinal cord is looked upon as the source of the tetanic spasms, it is but rational to assume that the true source is in the motor ganglia cells of the anterior horns, and that there exists a specific affinity in these cells for the tetanic toxins.

If this theory for the mechanism of general tetanus is accepted, we must still find a cogent and acceptable explanation for the local symptoms which arise constantly and without exception in experimental tetanus on animals, and, as already stated, probably also in man. If we assume what at first sight seems most probable, that the toxins generated by the bacilli at the point of infection are absorbed and get into the general circulation, then the spasms would necessarily be general and symmetrical from the very onset, or, at all events, without any special seat of predilection; but the fact that local tetanus constantly arises in animal experiments upsets this theory. This local tetanus received at first the explanation that it arises as a result of an irritation from the wound in the muscles nearest to the point of infection, either in consequence of the local action of the bacteria or of the wound itself, or its secretions. The probability, however, is far greater that the toxins are carried along the neighboring nerves to the spinal cord, and primarily excite to greater reflex irritability that segment of the cord in which these nerves take their origin. The

inoculation into a nerve-trunk proper by Tizzoni and Cattani has also given positive results.

From these experiments, we may assume with a certain degree of probability that the tetanic toxins assert their action in that place primarily and most quickly where they are first deposited in a somewhat concentrated form; and, as it has been proven that the peripheral nerves are not the seat of the infective process, then we must also presume that the toxins must first be taken by the channels of the peripheral nerves to the corresponding spinal segment. Proof for this would be positive, if we would constantly find the toxins in the peripheral nerves, and if we could constantly induce tetanus by implanting bits of the peripheral nerves into animals. As a matter of fact, this, however, does not occur constantly, which point is explained by Wassermann and Takaki [33] by the fact that the normal brain and cord have a certain tetanus antitoxic power.

The hypothesis of nerve conduction for the tetanic poison is therefore still without a solid foundation, particularly when it is taken into consideration that there still remains, at least in animals, one constant method of conduction for the tetanus poison, *i.e.*, the circulation, because in all animal experiments the blood has always been found to have tetanus toxic properties. To carry out, however, the hypothesis of nerve conduction, we are compelled to assume as correct the theory of Gumprecht (*loc. cit.*), that there are in every case two methods of dissemination for the toxins, one, the first one, along the peripheral nerves to the spinal cord, which is the cause of the so-called local tetanus, followed after a shorter or longer interval by general tetanus, and caused by infection of the central nervous system through the channel of the circulation. The fact that, when the intoxication is but a mild one, the entire process may be limited to the local tetanus would add additional weight to this hypothesis.

Of late, Stintzing (*loc. cit.*) has published a series of observations which tend to throw light on some of the mooted questions of tetanus. He investigated the toxic properties of the cerebrospinal fluid obtained by means of lumbar

puncture in two grave cases of tetanus. Inoculation of this cerebrospinal fluid into mice was always followed by true tetanus, but with the remarkable fact that it occurred at different periods; the incubation period being respectively one, two, nine, and twenty-six days. This led to the one assumption that the cerebrospinal fluid had various degrees of toxicity; another remarkable fact which Stintzing has observed in both these cases is that, contrary to animal experiments, the blood of these patients inoculated into animals did not prove to be toxic. This, however, is not surprising, as similar observations have previously been noted by Moritz,[34] Henoch,[35] Engelmann,[36] Kallmeyer,[37] and Tauber;[38] while a positive result was obtained by very few observers only, as Blumenthal and a few others. Stintzing, from this observation, though he will not deny the toxicity of the blood, is quite positive that the cerebrospinal fluid always contains the toxins in more active and in stronger concentration than does the blood.

If Stintzing's observation is proven to be a fact, then the theory of nerve conduction receives a stronger foundation in the greater and more constant toxicity of the cerebrospinal fluid; particularly if we take into consideration the anatomical fact that the subarachnoidal space which contains the cerebrospinal fluid is always in communication on one side with the interstices of the perineurium externum and internum, and on the other side with the interstices of the spinal cord.

One would naturally expect that so important a point should and could be also proven by animal experiment; but there are almost insurmountable difficulties because of the impossibility to obtain large quantities of cerebrospinal fluid by lumbar puncture in consequence of the small calibre of the spinal canal in animals.

If the presumption be a correct one, that the tetanus toxins are brought to the subarachnoidal space, respectively to the spinal cord, by means of the perineural and endoneural lymph channels, and so exert their toxic influence, it would still not explain the occurrence of local tetanus. It could be said, in counterargument, that the toxins may become rapidly

disseminated through the subarachnoidal space, and that consequently they act generally, but not locally, on the cord. But this is counteracted by the fact, as Stintzing (*loc. cit.*) explains it, that the production of the toxins takes place but slowly at the seat of infection, that therefore the inflow of toxins occurs only slowly, so to say, drop by drop. It is therefore not at all surprising that the toxins are taken up at once on their entrance by the nearest cells of the anterior horns, because of their specific affinity for this poison, before they had an opportunity to become diffused, and in this manner produced at first the "local" tetanus. Following out this line of argument, the later regional progress of the contractions, *i.e.*, at first in a transverse, then in ascending and descending direction, could be well explained; because it could be assumed that, after a saturation of the nearest motor cells, the poison would spread to adjoining groups. The fact that occasionally, in milder cases, the process is limited to the group of muscles first affected could also be brought into harmony by the assumption that only sufficient poison was produced to saturate the first group of cells.

This hypothesis, which, however, has a large amount of probability, would fully explain all the phenomena of experimental tetanus in animals, and for that matter also those of tetanus in men, with the exception that local tetanus is not observed so regularly in men. Stintzing attempts a very plausible explanation of this phenomenon, also, in the difference in size of the subarachnoidal space in men and animals, as it is evident that the toxins would be more slowly diffused in the comparatively narrow and tight channel of animals than in the wider channel of men. The rapid diffusion after its influx in men would also explain the early distribution of the spasms.

Stintzing sums up his research in the following: "The tetanus bacillus produces toxins at the seat of infection. These toxins get partly into the circulation (in animals surely) and may become active through this channel; as a rule, however, the toxins are carried along the nearest nerves, presumably in the meshes of the perineurium and endoneurium to the spinal

cord. On reaching the subarachnoidal space of the cord they produce in animals their toxic action at first at the point of entrance into the cord, and so cause the "local" tetanus. If sufficient poison is brought to the spinal cord, it produces next a regionary and, finally, general tetanus. The same *may* be true for human tetanus. Most frequently, however, in man the spasms are produced without any order, presumably because the toxins are diffused rapidly through the comparatively larger and loosely fitting subarachnoidal space. The point of attack for the toxins is certainly the motor ganglia cells of the anterior horns, which get into a state of increased reflex irritability by the action of the toxins.

The prognosis of tetanus is of the greatest importance in any given case; observation of a large number of cases, both in peace and war surgery, has taught us amply that the prognosis of any given case is particularly dependent upon two factors; viz.:

(1) The period of incubation.

(2) The rapidity of development of the symptoms, *i.e.*, the progress of the disease.

Regarding the first point, which can be obtained with the utmost accuracy in a majority of the cases, experience has taught that the shorter the period of incubation the worse is the prognosis; this statement is made in general, as in a measure, though a subordinate one, it is also dependent upon the second factor; but the observation in general has also shown that usually cases with a briefer period of incubation are also those in which the development of the symptoms is more acute and progress more rapid.

Many scattered statistical reports regarding the prognosis of tetanus are found in the literature. I will mention here only those found most frequently quoted.

Richter, quoted by Rotter,[39] in a statistic of 224 cases of tetanus following mostly wounds and injuries during the Franco-Prussian war, gives the following values in regard to prognosis:

Of 25 cases with a period of incubation of 1-5 days there were 4 per cent. recoveries.

Of 91 cases with a period of incubation of 6-10 days there were 4.4 per cent. recoveries.

Of 54 cases with a period of incubation of 11-15 days there were 27 per cent. recoveries.

Of 20 cases with a period of incubation of 15-20 days there were 45 per cent. recoveries.

Of 15 cases with a period of incubation of over 20 days there were 20 per cent. recoveries.

Almost similar values have been obtained by Poland (quoted by Rose [40]), who has collected his statistics from various London hospitals, viz.:

25 cases with a period of incubation of 1-5 days gave 4 per cent. recoveries.

61 cases with a period of incubation of 1-10 days gave 3.3 per cent. recoveries.

44 cases with a period of incubation of 10-22 days gave 25 per cent. recoveries.

6 cases with a period of incubation of over 22 days gave 50 per cent recoveries.

Richter, in a collection of 717 cases of tetanus caused by various injuries of war surgery, records 631 deaths, or a mortality of 88 per cent., with 40 recoveries, equalling 12 per cent.; and of these 40, 13 were of a milder variety.

Behring gives for tetanus a mortality of 80-90 per cent.

Raymond gives for tetanus a mortality of 90.5 per cent.

Fronz gives for Tetanus neonatorum a mortality of 50 per cent.

Larrey gives for Tetanus neonatorum a mortality of 50 per cent.

The records of the Bürger Hospital at Cologne give for tetanus a mortality of 62.5 per cent.

Garrigues [41] gives for 57 cases of puerperal tetanus a mortality of 84-92 per cent.

Gowers [42] gives for traumatic tetanus a mortality of 90 per cent.

Dean [43] gives for all cases of tetanus in various London hospitals, for a period of sixteen years, a mortality of 80 per cent.

A special committee,[44] appointed by the *British Medical Journal,* came to the conclusion that acute tetanus is incurable, and that, although anodynes and hypnotics sometimes afforded alleviation, there was known no remedy for it. They also found that between 1875 and 1892 there occurred in England and Wales 2969 deaths from traumatic tetanus, and between 1881 and 1892, 568 deaths from so-called idiopathic tetanus.

That tetanus is quite common and quite commonly fatal is shown also by the quotation [45] that there occurred in Greater New York during 1898, 73 deaths from tetanus.

Albertoni,[46] in a collection gathered by one of his students, gives a remarkable statistic in which he claims that tetanus is not the fatal disease it is claimed to be, and for 176 cases treated with 46 methods(?) of treatment gives 139 recoveries; equalling a mortality percentage of 21.1 per cent., and a percentage of recoveries of 78.9 per cent.

With the exception of the last quoted figures, all statistics show almost conclusively that when the period of incubation is very short, less than ten days, the percentage of recoveries is very small, on an average no more than 5 per cent.; and also that the prognosis improves with each day beyond this period, and may reach even as high as 50 per cent.

The above figures are fair examples, and may be considered as correct up to the last decennium. The prognosis of tetanus, however, certainly needs some revision in the light of modern treatment, *i.e.,* since the introduction of serum therapy in the treatment of tetanus. Many cases are reported as cured even when the period of incubation has been of a shorter duration than ten days.

Of the various statistics collected since the introduction of the antitoxin, I will only mention the following:

Marson [47] publishes the statistics of 38 cases, collected from different observers, with a mortality of 13 or 34.2 per cent.

Hewlet [48] collected 42 cases treated with antitoxin, with a mortality of 36 per cent.

Engelmann [30] publishes a statistic of 54 cases, treated with antitoxin of different makes (36 with Tizzoni's, 5 with Behring's, and 13 unnamed) with a mortality of 16, or 29.63 per cent.

Kanthack [49] collected 54 cases, of which 20 died, or a mortality of 37.03 per cent.

Wellner [50] collected 94 cases, of which 41 died, or a mortality of 45 per cent.

Köhler [51] collected 96 cases, of which 33 died and 63 recovered, or a mortality of 34.3 per cent.

Weischer [52] collected 98 cases, with a mortality of 41.8 per cent.

Lambert [53] collected 114 cases, of which 46 died, or a mortality of 40.35 per cent.

Lund [54] collected 167 cases, of which 54 died, or a mortality of 39.5 per cent.

Holsti [55] collected 171 cases, of which 74 died, or a mortality of 43.2 per cent.

After a painstaking and extensive search in the literature of the past ten years, utilizing for this purpose all the publications at my command, in which there was a possibility of a case being reported, I have been able to collect the following cases:

CASES TREATED BY SUBCUTANEOUS OR INTRAVENOUS INJECTIONS.

No. 1.—*Name*, Schwartz.[53] *Year*, 1891. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of forearm. *Period of incubation*, fifteen days. *Day of first injection*, fourteenth day. *Method of administration*, subcutaneous. *Amount*, 1.0. *Make*, Tizzoni. *Other treatment*, chloral. *Result*, recovery.

No. 2.—*Name*, Baginsky.[56] *Year*, 1891. *Diagnosis*, Tetanus neonatorum. *Nature of injury*, infection of navel. *Period of incubation*, eighth day of life. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 1.5. *Make*, Tizzoni, serum of immunized rabbit. *Other treatment*, not stated. *Result*, death. *Remarks*. Author says he never saved a case of Tetanus neonatorum; although Henoch, Saltmann, and Monti claim to have done so with chloral, physostigma, and musk.

No. 3.—*Name,* Finotti.[87] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed injury of hand. *Period of incubation,* eleven days. *Day of first injection,* third day. *Method of administration,* subcutaneous. *Amount,* 4.75. *Make,* Tizzoni, dog's serum. *Amount,* 0.40. *Make,* Tizzoni, rabbit's serum. *Other treatment,* morphine. *Result,* recovery.

No. 4.—*Name,* Finotti.[88] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* compound fracture of forearm. *Period of incubation,* fifteen days. *Day of first injection,* first day. *Method of administration,* subcutaneous. *Amount,* 4.80. *Make,* Tizzoni. *Other treatment,* none. *Result,* recovery. *Remarks.* Author says, to judge from the symptoms, a very bad case, in spite of the long period of incubation; recovery due entirely to the antitoxin.

No. 5.—*Name,* Berger.[89] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* injury of little finger. *Period of incubation,* fourteen days. *Day of first injection,* thirty-eighth day. *Method of administration,* subcutaneous. *Amount,* not stated. *Make,* Roux. *Other treatment,* chloral, morphine. *Result,* recovery. *Remarks.* Evidently a very mild case, if patient lived thirty-eight days after the onset of the symptoms. Author will not say whether recovery was due to the antitoxin or to the amputation.

No. 6.—*Name,* Polaillon.[90] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* injury of leg. *Period of incubation,* three weeks. *Day of first injection,* not stated. *Method of administration,* subcutaneous. *Amount,* not stated. *Make,* not stated. *Other treatment,* not stated. *Result,* death. *Remarks.* According to author, a medium grave case.

No. 7.—*Name,* Taruffi.[91] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* lacerated wound of little finger. *Period of incubation,* eleven days. *Day of first injection,* second day. *Method of administration,* subcutaneous. *Amount,* 1.5. *Make,* Tizzoni. *Other treatment,* not stated. *Result,* recovery. *Remarks.* Author says recovery was undoubtedly due to the antitoxin.

No. 8.—*Name,* Casali.[92] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* injury of foot by a piece of wood, followed by a phlegmon and lymphangitis. *Period of incubation,* eight days. *Day of first injection,* seventh day. *Method of administration,* subcutaneous. *Amount,* 1.40 cubic centimetres. *Make,* Tizzoni. *Other treatment,* chloral. *Result,* recovery. *Remarks.* Author says recovery was due solely to the antitoxin, in spite of the fact that it was used comparatively late.

No. 9.—*Name,* Tizzoni.[93] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed wound of finger. *Period of incubation,* twelve days. *Day of first injection,* tenth day. *Method of administration,* subcutaneous. *Amount,* 37 cubic centimetres and 1.35 dry. *Make,* Tizzoni. *Other treatment,* not stated. *Result,* recovery.

No. 10.—*Name,* Renon.[94] *Year,* 1892. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* incised wound of posterior auricular region. *Period of incubation,* six days. *Day of first injection,* first day. *Method*

of administration, subcutaneous. *Amount*, 57 cubic centimetres. *Make*, Tizzoni, rabbit's serum. *Other treatment*, not stated. *Result*, death.

No. 11.—*Name*, Renon.[84] *Year*, 1892. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, crushed wound of little finger. *Period of incubation*, seven days. *Day of first injection*, fourth day. *Method of administration*, subcutaneous. *Amount*, 80 cubic centimetres. *Make*, Tizzoni, rabbit's serum. *Other treatment*, chloral. *Result*, death.

No. 12.—*Name*, Pacini.[85] *Year*, 1892. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, incised wound of finger, caused by a scythe. *Period of incubation*, ten days. *Day of first injection*, fifteenth day. *Method of administration*, subcutaneous. *Amount*, 2.0. *Make*, Tizzoni. *Other treatment*, chloral. *Result*, recovery.

No. 13.—*Name*, Gagliardi.[86] *Year*, 1892. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of foot. *Period of incubation*, twelve days. *Day of first injection*, twelfth day. *Method of administration*, subcutaneous. *Amount*, 1.05. *Make*, Tizzoni. *Other treatment*, morphine, chloral, Baccelli. *Result*, recovery.

No. 14.—*Name*, Finotti.[87] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of neck by a piece of wood. *Period of incubation*, about twenty-three days. *Day of first injection*, fifth day. *Method of administration*, subcutaneous. *Amount*, 2.70. *Make*, Tizzoni. *Other treatment*, some morphine, some chloral. *Result*, recovery. *Remarks.* No tetanus bacilli could be cultivated from the wound; but they were cultivated from the wood removed from the wound. Author thinks that recovery was due entirely to the antitoxin.

No. 15.—*Name*, Lesi.[88] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, incised wound of foot, caused by a piece of glass. *Period of incubation*, six days. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 100 cubic centimetres. *Make*, Tizzoni. *Other treatment*, chloral, antipyrine, pilocarpine, but none after injections were begun. *Result*, recovery. *Remarks.* Author says it was a bad case in all respects, followed by ultimate recovery, which was unquestionably due to the antitoxin.

No. 16.—*Name*, Henoch.[89] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, wound of hand. *Period of incubation*, not obtainable. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 30 cubic centimetres. *Make*, Behring. *Other treatment*, morphine, anæstheties. *Result*, death. *Remarks.* Author says that the death in this case does not in the least speak against the use of antitoxin.

No. 17.—*Name*, Moritz.[100] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, numerous wounds on both hands. *Period of incubation*, not obtainable. *Day of first injection*, eighth day. *Method of administration*, subcutaneous. *Amount*, 95.0. *Make*, Behring. *Other treatment*, chloral, morphine. *Result*, recovery. *Remarks.* Author says that, judging from the symptoms, this case belongs to the more chronic or subacute variety.

No. 18.—*Name*, von Ranke.[101] *Year*, 1893. *Diagnosis*, Tetanus trau-

maticus. *Nature of injury*, injury of foot, caused by a piece of wire. *Period of incubation*, about three weeks. *Day of first injection*, fifth day. *Method of administration*, subcutaneous. *Amount*, 50 cubic centimetres. *Make*, Behring. *Other treatment*, chloral. *Result*, recovery. *Remarks*, Author will not say what effect the antitoxin had, as a good prognosis was given even before its use.

No. 19.—*Name*, von Ziemssen.[102] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of foot, caused by a piece of glass. *Period of incubation*, seven to eight days. *Day of first injection*, fifteenth day. *Method of administration*, subcutaneous. *Amount*, 100 cubic centimetres. *Make*, Behring. *Other treatment*, purposely none. *Result*, recovery. *Remarks*. Author says, only a medium grave case, with no unfavorable prognosis; hence he will not give too much credit to the antitoxin, and believes case would have recovered even without it.

No. 20.—*Name*, Brunner.[103] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, punctured wound of foot, caused by a nail. *Period of incubation*, eight days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 100 cubic centimetres. *Make*, Behring. *Other treatment*, morphine. *Result*, death. *Remarks*. Author says undoubtedly a bad case; is not at all enthusiastic about the antitoxin.

No. 21.—*Name*, Baginsky.[104] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of tongue, not diphtheritic. *Period of incubation*, unknown. *Day of first injection*, fifth day. *Method of administration*, subcutaneous. *Amount*, 72 cubic centimetres. *Make*, Behring. *Other treatment*, chloral, etc. *Result*, recovery. *Remarks*. Case was, however, also complicated by true diphtheria.

No. 22.—*Name*, Escherich.[105] *Year*, 1893. *Diagnosis*, Tetanus neonatorum. *Nature of injury*, infection of umbilicus. *Period of incubation*, eight days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 0.03. *Make*, Tizzoni. *Other treatment*, chloral. *Result*, death.

No. 23.—*Name*, Escherich.[105] *Year*, 1893. *Diagnosis*, Tetanus neonatorum. *Nature of injury*, infection of umbilicus. *Period of incubation*, twelve days. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 0.5. *Make*, Tizzoni. *Other treatment*, chloral. *Result*, death.

No. 24.—*Name*, Escherich.[105] *Year*, 1893. *Diagnosis*, Tetanus neonatorum. *Nature of injury*, infection of umbilicus. *Period of incubation*, eleven days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 0.9. *Make*, Tizzoni. *Other treatment*, not stated. *Result*, recovery.

No. 25.—*Name*, Escherich.[105] *Year*, 1893. *Diagnosis*, Tetanus neonatorum. *Nature of injury*, infection of umbilicus. *Period of incubation*, five days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 0.9. *Make*, Tizzoni. *Other treatment*, not stated. *Result*, death.

No. 26.—*Name*, Gattai.[106] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, punctured wound of thumb. *Period of incubation*, six days. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 22 cubic centimetres. *Make*, Tizzoni, rabbit's serum, also 475 cubic centimetres; Tizzoni, dog's serum, and 29 cubic centimetres; Tizzoni, horse's serum. *Other treatment*, chloral. *Result*, recovery. *Remarks*. Author says that, judging from the period of incubation and symptoms, it was a very bad case; recovery due only to early use and large quantity of antitoxin.

No. 27.—*Name*, Magagni.[107] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, contused wound of toe. *Period of incubation*, eight days. *Day of first injection*, seventh day. *Method of administration*, subcutaneous. *Amount*, 2.75. *Make*, Tizzoni. *Other treatment*, chloral. *Result*, recovery.

No. 28.—*Name*, Buschke and Oergel.[108] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, compound fracture of leg, caused by kick of a horse. *Period of incubation*, nine days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 10 cubic centimetres. *Make*, Behring. *Other treatment*, not stated. *Result*, death. *Remarks*. Patient survived injection only one-half an hour.

No. 29.—*Name*, Rotter.[109] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of hand. *Period of incubation*, eight days. *Day of first injection*, sixth day. *Method of administration*, subcutaneous. *Amount*, 261 cubic centimetres. *Make*, Behring. *Other treatment*, 0.01 morphine once only. *Result*, recovery. *Remarks*. Author says recovery was due solely to the use of antitoxin, as only one dose of morphine was given.

No. 30.—*Name*, Barth.[110] *Year*, 1893. *Diagnosis*, Tetanus(?). *Nature of injury*, unknown. *Period of incubation*, unknown. *Day of first injection*, seventh day. *Method of administration*, subcutaneous. *Amount*, 275 cubic centimetres. *Make*, Behring. *Other treatment*, chloral and KBr. *Result*, recovery. *Remarks*. Author says that, judging from symptoms and period of incubation, it was a very bad case; regrets his inability to find seat of infection.

No. 31.—*Name*, Roux and Vaillard.[111] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, extraction of tooth. *Period of incubation*, fifteen days. *Day of first injection*, fourth day. *Method of administration*, subcutaneous. *Amount*, 147 cubic centimetres. *Make*, Roux. *Other treatment*, chloral. *Result*, death.

No. 32.—*Name*, Roux and Vaillard.[111] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, cartridge injury. *Period of incubation*, eight days. *Day of first injection*, fourteenth day. *Method of administration*, subcutaneous. *Amount*, 108 cubic centimetres. *Make*, Roux. *Other treatment*, not stated. *Result*, death.

No. 33.—*Name*, Roux and Vaillard.[111] *Year*, 1893. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, crushed wound of hand. *Period of incubation*, five days. *Day of first injection*, first day. *Method of administration*, subcutaneous, intravenous. *Amount*, 20 cubic centimetres.

10 cubic centimetres. *Make,* Roux. *Other treatment,* not stated. *Result,* death.

No. 34.—*Name,* Roux and Vaillard.[111] *Year,* 1893. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* numerous (engine) injuries. *Period of incubation,* eight days. *Day of first injection,* second day. *Method of administration,* subcutaneous. *Amount,* 402 cubic centimetres. *Make,* Roux. *Other treatment,* chloral, morphine. *Result,* death.

No. 35.—*Name,* Roux and Vaillard.[111] *Year,* 1893. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* splinter injury of finger. *Period of incubation,* fourteen days. *Day of first injection,* second day. *Method of administration,* subcutaneous. *Amount,* 247 cubic centimetres. *Make,* Roux. *Other treatment,* chloral. *Result,* death.

No. 36.—*Name,* Roux and Vaillard.[111] *Year,* 1893. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* injury of hand. *Period of incubation,* fifteen days. *Day of first injection,* third day. *Method of administration,* subcutaneous. *Amount,* 265 cubic centimetres. *Make,* Roux. *Other treatment,* chloral. *Result,* recovery.

No. 37.—*Name,* Berger.[112] *Year,* 1893. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* unknown. *Period of incubation,* not stated. *Day of first injection,* second day. *Method of administration,* subcutaneous. *Amount,* 280 cubic centimetres. *Make,* serum of immune horse. *Other treatment,* large doses of chloral. *Result,* death.

No. 38.—*Name,* Dean.[113] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed wound of finger. *Period of incubation,* twenty-five days. *Day of first injection,* fifth day. *Method of administration,* subcutaneous. *Amount,* 15.75. *Make,* Tizzoni. *Other treatment,* morphine, chloral. *Result,* recovery. *Remarks.* Author will not express an opinion regarding the severity of the case; believes the antitoxin was quite an aid in the treatment.

No. 39.—*Name,* Evans,[114] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* incised wound over knee. *Period of incubation,* eight days. *Day of first injection,* tenth day. *Method of administration,* subcutaneous. *Amount,* 4.5. *Make,* Tizzoni. *Other treatment,* morphine, chloral, bromides. *Result,* recovery.

No. 40.—*Name,* Fanning.[115] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* punctured wound of foot, caused by stepping on a nail. *Period of incubation,* eight days. *Day of first injection,* first day. *Method of administration,* subcutaneous. *Amount,* not stated. *Make,* Roux. *Other treatment,* not stated. *Result,* death. *Remarks.* Author says death resulted in spite of the early use of antitoxin.

No. 41.—*Name,* Parker.[116] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* splinter injury of thumb. *Period of incubation,* four to five weeks. *Day of first injection,* not stated. *Method of administration,* subcutaneous. *Amount,* 5.625. *Make,* not stated. *Other treatment,* Baccelli. *Result,* recovery. *Remarks.* Undoubtedly a case of chronic tetanus; but the antitoxin was of considerable value, according to author.

No. 42.—*Name,* Clarke.[117] *Year,* 1894. *Diagnosis,* Tetanus trau-

matiens. *Nature of injury,* crushed wound of thumb. *Period of incubation,* one week. *Day of first injection,* fourth day. *Method of administration,* subcutaneous. *Amount,* 15.0. *Make,* Roux. *Other treatment,* chloral and KBr. *Result,* recovery. *Remarks.* Author says it is only reasonable to ascribe the recovery to the antitoxin, as the drugs appeared to have little or no effect.

No. 43.—*Name,* Paget.[118] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* not stated. *Period of incubation,* not stated. *Day of first injection,* not stated. *Method of administration,* subcutaneous. *Amount,* not stated. *Make,* Roux. *Other treatment,* not stated. *Result,* death.

No. 44.—*Name,* Ginsti and Bouainti.[119] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* extensive injuries of face and body after railroad collision. *Period of incubation,* twenty-two days. *Day of first injection,* fourth day. *Method of administration,* subcutaneous. *Amount,* 80.0. *Make,* Tizzoni, horse's serum, also 110 cubic centimetres. *Make,* Tizzoni, dog's serum. *Other treatment,* chloral. *Result,* recovery. *Remarks.* Author says that, judging from symptoms, it was a very bad case, cured only by the antitoxin.

No. 45.—*Name,* Bauer.[120] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* splinter injury of foot. *Period of incubation,* seven days. *Day of first injection,* third day. *Method of administration,* subcutaneous. *Amount,* 2.25. *Make,* Tizzoni. *Other treatment,* chloral. *Result,* death. *Remarks.* Patient survived injection only by a few hours.

No. 46.—*Name,* Doerfler.[121] *Year,* 1894. *Diagnosis,* Tetanus(?). *Nature of injury,* unknown. *Period of incubation,* unknown. *Day of first injection,* tenth day. *Method of administration,* subcutaneous. *Amount,* 50 cubic centimetres. *Make,* Behring. *Other treatment,* chloral and morphine. *Result,* recovery. *Remarks.* Author says, a medium grave case with good prognosis, and will not draw conclusions regarding the efficacy of the antitoxin.

No. 47.— *Name,* E. Schwartz.[122] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* pustule of leg. *Period of incubation,* unknown. *Day of first injection,* second day. *Method of administration* subcutaneous. *Amount,* 4.0. *Make,* Tizzoni. *Other treatment,* not stated. *Result,* death. *Remarks.* Patient died suddenly. Autopsy showed parenchymatous degeneration of myocardium.

No. 48.—*Name,* Tavel.[123] *Year,* 1894. *Diagnosis,* Tetanus cephalicus. *Nature of injury,* wound of face, caused by kick of a horse. *Period of incubation,* seven days. *Day of first injection,* fourth day. *Method of administration,* subcutaneous. *Amount,* 120 cubic centimetres. *Make,* Tavel. *Other treatment,* chloral. *Result,* recovery.

No. 49.—*Name,* Remesoff and Fedoroff.[124] *Year,* 1894. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* punctured wound of foot, caused by stepping on a nail. *Period of incubation,* about eight days. *Day of first injection,* sixth day. *Method of administration,* subcutaneous. *Amount,* 200 cubic centimetres. *Make,* author's. *Other treatment,* chloral and NaBr. *Result,* recovery.

No. 50.—*Name*, Remesoff and Fedoroff.[124] *Year*, 1894. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, possibly from scratch of a cat. *Period of incubation* unknown. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 150 cubic centimetres. *Make*, author's. *Other treatment*, chloral and NaBr. *Result*, death. *Remarks*. Cause of death, pneumonia.

No. 51.—*Name*, von Hacker.[123] *Year*, 1894. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, crushed wound of palm. *Period of incubation*, eleven days. *Day of first injection*, seventh day. *Method of administration*, subcutaneous. *Amount*, 8.85. *Make*, Tizzoni. *Other treatment*, narcotics. *Result*, recovery. *Remarks*. Author says that both were bad cases, in spite of the apparently long period of incubation.

No. 52.—*Name*, von Hacker.[123] *Year*, 1894. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of thumb. *Period of incubation*, unknown. *Day of first injection*, fifth day. *Method of administration*, subcutaneous. *Amount*, 4.05. *Make*, Tizzoni. *Other treatment*, not stated. *Result*, recovery.

No. 53.—*Name*, Marson.[126] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, compound fracture of thumb. *Period of incubation*, ten days. *Day of first injection*, sixth day. *Method of administration*, subcutaneous. *Amount*, 136 grains. *Make*, not stated. *Other treatment*, chloral, KBr, physostigma. *Result*, death. *Remarks*. Author believes there was a beneficial effect of the antitoxin on the spasms; and gives expression to the thought that the death may have been due to sepsis.

No. 54.—*Name*, Marriott.[127] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of chin. *Period of incubation*, six days. *Day of first injection*, seventh day. *Method of administration*, subcutaneous. *Amount*, 8.7. *Make*, Tizzoni. *Other treatment*, chloral, morphine, physostigma. *Result*, recovery. *Remarks*. Author thinks recovery was due to the antitoxin.

No. 55.—*Name*, Fenwick.[125] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, contused wound of thumb. *Period of incubation*, ten days. *Day of first injection*, thirteenth day. *Method of administration*, subcutaneous. *Amount*, 16.055. *Make*, not stated. *Other treatment*, chloral, morphine. *Result*, recovery.

No. 56.—*Name*, Williamson.[129] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, extensive burns and lacerated wound of buttock. *Period of incubation*, eleven days. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 111 grains. *Make*, Tizzoni. *Other treatment*, morphine. *Result*, death. *Remarks*. Author says that the antitoxin appeared to be neither beneficial nor hurtful; the disease, though slow, pursuing an ordinary course. Although the treatment was begun early, its failure was probably due to even that period being too late.

No. 57.—*Name*, Gornall.[130] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of leg. *Period of incubation*, twelve days. *Day of first injection*, second day. *Method of administra-*

tion, subcutaneous. *Amount*, 11.0. *Make*, Tizzoni. *Other treatment*, chloral and KBr. *Result*, recovery.

No. 58.—*Name*, Turner and Cheatle.[131] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of thumb by a barbed wire. *Period of incubation*, about eight days. *Day of first injection*, eighth day. *Method of administration*, subcutaneous. *Amount*, 3.5. *Make*, British Institute of Preventive Medicine. *Other treatment*, not stated. *Result*, recovery. *Remarks*. Author says that, judging from period of incubation, the case was a grave one, but from the symptoms it was of a milder type. But he also says that no drug would have arrested the disease like the antitoxin did.

No. 59.—*Name*, Farrant.[132] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, wound of face, caused by kick of a horse. *Period of incubation*, five days. *Day of first injection*, tenth day. *Method of administration*, subcutaneous. *Amount*, 74 grains. *Make*, British Institute of Preventive Medicine. *Other treatment*, chloral, KBr, morphine, etc. *Result*, death.

No. 60.—*Name*, Tirard.[133] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, wound of foot, caused by a piece of glass. *Period of incubation*, about a fortnight. *Day of first injection*, about tenth day. *Method of administration*, subcutaneous. *Amount*, 60 grains. *Make*, British Institute of Preventive Medicine. *Other treatment*, chloral. *Result*, recovery. *Remarks*. Author says that certainly after the antitoxin the child was more peaceful and the opisthotonos spasm was less.

No. 61.—*Name*, Hartley.[134] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, wound of forearm, caused by a nail. *Period of incubation*, thirteen days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 8.0. *Make*, British Institute of Preventive Medicine. *Other treatment*, chloral, KBr, hyoscyamus, cannabis indica. *Result*, recovery. *Remarks*. Author says it is doubtful whether either the antitoxin or the chloral had anything to do with the favorable result.

No. 62.—*Name*, Oelberg.[135] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, splinter injury of foot. *Period of incubation*, about fourteen days. *Day of first injection*, fourth day. *Method of administration*, subcutaneous. *Amount*, 1.65. *Make*, Tizzoni. *Other treatment*, large doses of morphine and chloral. *Result*, death.

No. 63.—*Name*, Firth.[136] *Year*, 1895. *Diagnosis*, Tetanus neonatorum. *Nature of injury*, infection of umbilicus. *Period of incubation*, eight days. *Day of first injection*, fourth day. *Method of administration*, subcutaneous. *Amount*, 2.0. *Make*, not stated. *Other treatment*, KBr and chloral. *Result*, death. *Remarks*. Author says no improvement whatsoever followed the injections.,

No. 64.—*Name*, Pel.[137] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, slight injury of foot. *Period of incubation*, eight days. *Day of first injection*, sixth day. *Method of administration*, subcutaneous. *Amount*, 9.0. *Make*, Tizzoni. *Other treatment*, not stated. *Result*, recovery. *Remarks*. Author says that recovery was not dependent upon the treatment.

No. 65.—*Nome*, Granowsky.[138] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, splinter injury of palm. *Period of incubation*, nine days. *Day of first injection*, thirteenth day. *Method of administration*, subcutaneous. *Amount*, 25 cubic centimetres. *Make*, Behring. *Other treatment*, chloral, NaBr. *Result*, recovery. *Remarks*. Case does not prove anything, as patient was almost well when injections were begun.

No. 66.—*Name*, Thompson.[139] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, wound of foot by iron spike. *Period of incubation*, about two and a half weeks. *Day of first injection*, not stated. *Method of administration*, subcutaneous. Toxins. *Result*, recovery. *Remarks*. Author gives the history of the case in detail up to the thirteenth day of the disease. On this day he says, "I succeeded in obtaining from the Loomis laboratory a tetanus toxin made after the method of Brieger, that is, it was developed by growing fresh tetanus germs in a strong bouillon, and the boy received daily for five days inoculations of from one-half to one cubic centimetre, which were placed in the gluteal region." Also chloral, morphine, urethan, conium, etc. Ultimately the case recovered completely. Regarding the benefit he obtained, the author says, "I confess myself somewhat in doubt in regard to it; they (the injections) certainly did no harm."

It is true, somewhat late in the disease cultures were made from the vicinity of the scar, result negative; negative results also on attempting a culture with the blood. But cultures made from the scrapings around the hole of the boot, and from the earth of the yard where the patient lived, did develop cultures of tetanus. (These experiments prove nothing, as cultures from a cicatrix and blood are not necessarily positive; while the other positive results may be so, nay, are very likely to be so; but the patient must not necessarily have tetanus.) Author also says that tetanus bacilli grow in all media, both with and without oxygen; but all observers agree that the tetanus bacillus is positively anaërobic.

Though author argues for the correctness of his diagnosis, and differentiates it from hysteria, it may have been a wrong diagnosis. Even if it was tetanus, it was not proven, as author believes, by the culture experiments. And if it was a case of tetanus, it could not have been cured by the injections, as the author injected tetanus toxins, not antitoxin.

No. 67.—*Nome*, Miti.[140] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, punctured wound of foot. *Period of incubation*, three days. *Day of first injection*, eleventh day. *Method of administration*, subcutaneous. *Amount*, 5.0. *Make*, Tizzoni. *Other treatment*, chloral. *Result*, recovery. *Remarks*. Author says unquestionably a very bad case, with very short period of incubation; cured only by the antitoxin.

No. 68.—*Nome*, Illuminati.[141] *Year*, 1895. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, wound of foot. *Period of incubation*, thirteen days. *Day of first injection*, seventh day. *Method of administration*, subcutaneous. *Amount*, 5.0. *Make*, Tizzoni. *Other treatment*, chloral. *Result*, recovery.

No. 69.—*Nome*, Douglas.[142] *Year*, 1894. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, dog-bite of thumb. *Period of incubation*, five days. *Day of first injection*, sixth day. *Method of administration*,

subcutaneous. *Amount,* ½ tube. *Make,* Tizzoni. *Other treatment,* chloral, morphine, eserine. *Result,* death. *Remarks.* Author argues for the diagnosis, though hydrophobia is not excluded. His arguments are the early appearance of the trismus, the absence of delirium, and the fact that the dog remained well up to the time of publication, six weeks after the accident. Author regrets not having used the antitoxin earlier.

No. 70.—*Name,* Caretti.[143] *Year,* 1895. *Diagnosis,* Tetanus cephalicus. *Nature of injury,* crushed and lacerated wound of temporal region. *Period of incubation,* eight days. *Day of first injection,* second day. *Method of administration,* subcutaneous. *Amount,* 9.0. *Make,* Tizzoni. *Other treatment,* chloral. *Result,* recovery.

No. 71.—*Name,* Walko.[144] *Year,* 1895. *Diagnosis,* Tetanus puerperalis. *Nature of injury,* tamponade of uterus for post-partum hæmorrhage. *Period of incubation,* nine days. *Day of first injection,* fourth day, *Method of administration,* subcutaneous. *Amount,* 3.6. *Make,* Tizzoni. *Other treatment,* none, on purpose. *Result,* death.

No. 72.—*Name,* Vagedes.[145] *Year,* 1895. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed wound of finger. *Period of incubation,* about eight days. *Day of first injection,* second day. *Method of administration,* subcutaneous. *Amount,* 30.0. *Make,* Behring. *Other treatment,* choral. *Result,* recovery. *Remarks.* Author says case was a mild one, hence will not say how much the recovery was due to the antitoxin.

No. 73.—*Name,* Preindlsberger.[146] *Year,* 1895. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed injury of finger. *Period of incubation,* six days. *Day of first injection,* third day. *Method of administration,* subcutaneous. *Amount,* 0.425. *Make,* Tizzoni. *Other treatment,* chloral. *Result,* death. *Remarks.* Tetanus bacilli found in the wound secretions.

No. 74.—*Name,* Preindlsberger.[146] *Year,* 1895. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed wound of foot. *Period of incubation,* thirteen days. *Day of first injection,* second day. *Method of administration,* subcutaneous. *Amount,* 7.39. *Make,* Tizzoni. *Other treatment,* chloral, morphine. *Result,* recovery. *Remarks,* Author will not say how far recovery was due to the antitoxin.

No. 75.—*Name,* Howlett.[147] *Year,* 1895. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* gunshot injury of leg. *Period of incubation,* nineteen days. *Day of first injection,* fifth day. *Method of administration,* subcutaneous. *Amount,* 22½ grains. *Make,* not stated. *Other treatment,* chloral, KBr, cannabis indica. *Result,* recovery. *Remarks.* Author praises the good effect of the antitoxin.

No. 76.—*Name,* Foges.[148] *Year,* 1895. *Diagnosis,* Tetanus (?). *Nature of injury,* not discoverable. *Period of incubation,* unknown. *Day of first injection,* sixth day. *Method of administration,* subcutaneous. *Amount,* 2.4. *Make,* Tizzoni. *Other treatment,* not stated. *Result,* death.

No. 77.—*Name,* Willemer.[149] *Year,* 1896. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* scratch wound of neck. *Period of incubation,* four days. *Day of first injection,* seventh day. *Method of administration,*

subcutaneous. *Amount*, 9.0. *Make*, Behring. *Other treatment*, morphine, chloral. *Result*, recovery. *Remarks*, Author looks upon the case as a grave one.

No. 78.—*Name*, Ridge.[150] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of finger and thumb. *Period of incubation*, thirteen days. *Day of first injection*, eighth day. *Method of administration*, subcutaneous. *Amount*, 13.0. *Make*, British Institute of Preventive Medicine. *Other treatment*, chloral, KBr. *Result*, recovery.

No. 79.—*Name*, Fenwick.[151] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of hand, with subsequent gangrene. *Period of incubation*, thirteen days. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 3.0. *Make*, not stated. *Other treatment*, morphine. *Result*, death. *Remarks*. Author thinks the antitoxin increased the spasms instead of diminishing them.

No. 80.—*Name*, Baker.[152] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of groin, inflicted by the horn of a buffalo. *Period of incubation*, some few days. *Day of first injection*, seventh day. *Method of administration*, subcutaneous. *Amount*, 3.0. *Make*, British Institute of Preventive Medicine. *Other treatment*, chloral, KBr, hyoscyamus, physostigma. *Result*, death. *Remarks*. Author says no amelioration followed the injections; on the contrary, patient got worse.

No. 81.—*Name*, Baker.[153] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, incised wound of leg, caused by a piece of glass. *Period of incubation*, ten days. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 6.5. *Make*, British Institute of Preventive Medicine. *Other treatment*, morphine. *Result*, death. *Remarks*. Author says the use of the antitoxin certainly did not appear to produce any amelioration of the symptoms.

No. 82.—*Name*, McEwan,[154] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, amputation of toe for injury. *Period of incubation*, ten days. *Day of first injection*, third day. *Method of administration*, subcutaneous. *Amount*, 100 cubic centimetres. *Make*, Paris Institute Pasteur. *Other treatment*, chloral. *Result*, death. *Remarks*. Author thinks both were severe cases; and says that, although the antitoxin was used early, it produced no amelioration of the symptoms.

No. 83.—*Name*, McEwan.[155] *Year*, 1896. *Diagnosis*, Tetanus puerperalis. *Nature of injury*, abortion. *Period of incubation*, seven days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 2.0. *Make*, Duncan and Flockhart, also 10 cubic centimetres. *Make*, Paris Institute Pasteur. *Other treatment*, chloral. *Result*, death.

No. 84.—*Name*, Greenwood.[156] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, gunshot wound of hand, compound fracture. *Period of incubation*, eleven days. *Day of first injection*, fourth day. *Method of administration*, subcutaneous. *Amount*, 162 grains. *Make*,

Tizzoni. *Other treatment*, various remedies. *Result*, recovery. *Remarks.* Author says a bad case, though he will not say that recovery was due to the antitoxin, he has seen improvement from its use.

No. 85.—*Name*, Williams.[156] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, compound fracture of radius and ulna. *Period of incubation*, four days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 60.0. *Mode*, not stated. *Other treatment*, not stated. *Result*, death.

No. 86.—*Name*, Macartney.[157] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, removal of epithelioma of vulva. *Period of incubation*, eight days. *Day of first injection*, sixth day. *Method of administration*, subcutaneous. *Amount*, minimum dose. *Make*, British Institute of Preventive Medicine. *Other treatment*, not stated. *Result*, death. *Remarks.* (Did infection occur at the time of the operation?)

No. 87.—*Name*, Macartney.[157] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, contused wound of ankle, caused by passage of a cart-wheel. *Period of incubation*, seven days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, three-fifths of adult dose. *Make*, not stated. *Other treatment*, chloral. *Result*, death. *Remarks.* Author says he has not seen the slightest effect from the antitoxin in either case.

No. 88.—*Name*, Macartney.[157] *Year*, 1896. *Diagnosis*, tetanus traumaticus. *Nature of injury*, not stated. *Period of incubation*, three or four days. *Day of first injection*, soon. *Method of administration*, subcutaneous. *Amount*, not stated. *Make*, not stated. *Other treatment*, not stated. *Result*, death.

No. 89.—*Name*, Bronner.[158] *Year*, 1896. *Diagnosis*, Tetanus(?). *Nature of injury*, not stated. *Period of incubation*, not stated. *Day of first injection*, not stated. *Method of administration*, subcutaneous. *Amount*, not stated. *Make*, not stated. *Other treatment*, chloral and KBr. *Result*, recovery.

No. 90.—*Name*, Tracey.[159] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, burn of forehead and leg. *Period of incubation*, fourteen days. *Day of first injection*, fifth day. *Method of administration*, subcutaneous. *Amount*, 4⅛. *Make*, Tizzoni. *Other treatment*, chloral, morphine, atropine. *Result*, recovery. *Remarks.* (Judging from description, evidently a mild case.)

No. 91.—*Name*, Farrant.[160] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, lacerated wound of palm; compound fracture of leg; amputation. *Period of incubation*, eight days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 10 grains. *Make*, British Institute of Preventive Medicine, also 59 grains, Tizzoni. *Other treatment*, not stated. *Result*, death. *Remarks.* (As amputation of the leg was performed only two hours after the accident, the infection very likely occurred from the palm.)

No. 92.—*Name*, Bienwald.[161] *Year*, 1896. *Diagnosis*, Tetanus(?). *Nature of injury*, not stated. *Period of incubation*, not stated. *Day of first injection*, second day. *Method of administration*, intravenous.

Amount, 5.0. *Make*, Behring. *Other treatment*, morphine. *Result*, death.

No. 93.—*Name*, Kocher.[102] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, contused wound of knee. *Period of incubation*, not stated. *Day of first injection*, not stated. *Method of administration*, not stated. *Amount*, not stated. *Make*, some English make. *Other treatment*, not stated. *Result*, recovery. *Remarks*. Author says prognosis was good in the case, and does not believe that it was the antitoxin which saved the life.

No. 94.—*Name*, Trevelyan.[103] *Year*, 1896. *Diagnosis*, Tetanus cephalicus. *Nature of injury*, injury to eyelids. *Period of incubation*, twelve days. *Day of first injection*, second day. *Method of administration*, subcutaneous. *Amount*, 1 tube. *Make*, Roux. *Other treatment*, morphine. *Result*, death. *Remarks*. Author says there was no improvement seen in this case from the antitoxin; but he still thinks that the future treatment of tetanus lies in this direction.

No. 95.—*Name*, De Palma.[104] *Year*, 1896. *Diagnosis*, Tetanus cephalicus. *Nature of injury*, extensive injuries of nose and face. *Period of incubation*, seven days. *Day of first injection*, third day. *Method of administration*, subcutaneous. *Amount*, 12.5. *Make*, Tizzoni. *Other treatment*, chloral, morphine. *Result*, recovery. *Remarks*. According to author, a very bad case.

No. 96.—*Name*, Cercignani.[105] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of hand, cobweb used as hæmostatic. *Period of incubation*, four days. *Day of first injection*, fifth day. *Method of administration*, subcutaneous. *Amount*, 80 cubic centimetres and 24.5. *Make*, Tizzoni. *Other treatment*, chloral, morphine. *Result*, recovery. *Remarks*. According to author, a very bad case; recovery due to the antitoxin.

No. 97.—*Name*, Baker.[106] *Year*, 1896. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, traumatic ulcer over ankle. *Period of incubation*, unknown. *Day of first injection*, fifteenth day. *Method of administration*, subcutaneous. *Amount*, 12.5. *Make*, not stated. *Other treatment*, not stated. *Result*, recovery.

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(TO BE CONTINUED.)